Assessment of new-generation glistening-free hydrophobic acrylic intraocular lens material

Christophe Pagnoulle, PhD, Dimitriya Bozukova, PhD, Laure Gobin, PhD, Virginie Bertrand, MSc, Marie-Claire Gillet-De Pauw, PhD

PURPOSE: To determine the hydrophobic, antiglistening, and bioadhesiveness properties of a new polymer, GF raw material, and to determine the suitability of this material for use in intraocular lenses (IOLs).

SETTING: University of Liege, Liege, Belgium.

DESIGN: Experimental study.

METHODS: Intraocular lenses made of the new hydrophobic acrylic material were tested and compared with reference acrylic materials. The stability of their polymer matrix was estimated by testing for glistenings. The relative surface hydrophobicity was quantified via contact-angle measurements. The degrees of bioadhesiveness of the reference and test materials were assessed by in vitro porcine lens epithelial cell (LEC) culture.

RESULTS: The glistening test showed that the new material had greater stability under worst-case conditions than previous-generation hydrophobic acrylic materials. The new polymer had the same hydrophobic properties as the hydrophobic Acrysof IQ SN60WF material; both materials were less hydrophobic than the hydrophobic Sensar AR40e material and more hydrophobic than the hydrophilic Ioflex IOL material. The in vitro bioadhesiveness tests showed that porcine LEC adhesion levels of the new material were intermediate with respect to those of the 2 reference hydrophobic materials.

CONCLUSIONS: When equilibrated in aqueous medium, the new-generation hydrophobic acrylic material reached a low water content at equilibrium, making it glistening free. The hydrophobicity and bioadhesiveness of the new raw material were comparable to those of state-of-the-art reference materials; these properties may resist the formation of posterior capsule opacification.

Financial Disclosure: Dr. Pagnoulle has a proprietary interest in the GF material. Drs. Pagnoulle, Gobin, and Bozukova are employees of Physiol S.A. Mme. V. Bertrand and Dr. Gillet-De Pauw have no financial or proprietary interest in any material or method mentioned.

J Cataract Refract Surg 2012; 38:1271–1277 © 2012 ASCRS and ESCRS

Cataract surgery is a well-established procedure during which the cataractous natural lens is extracted and replaced by an intraocular lens (IOL). Today, the preferable surgical technique is small-incision phacoemulsification, which is associated with a reduced risk for postoperative complications and with faster patient recovery.[1] With the discovery of this technique, foldable IOL materials were simultaneously developed to allow insertion of an IOL through a small, self-sealing incision.

Posterior capsule opacification (PCO) is a postoperative complication that remains a significant cause of visual impairment after surgery. Apart from the presence of a sharp or square 360-degree edge on the IOL optic,[2] PCO is significantly reduced by implanting IOLs of bioadhesive materials. This type of material provokes quick and firm contact between the IOL and the capsule, directly or indirectly via an intermediate layer of lens epithelial cells (LECs); this is known as the sandwich model of Linnola.[3] This behavior is typical of hydrophobic acrylic IOLs but not of hydrophilic acrylic (hydrogel) or silicone IOLs, and it provides the IOL with PCO resistance and rotational stability.

Hydrophobic acrylic IOLs are usually conditioned in their dry states before implantation, and the sudden change in environment (eg, in the average temperature and humidity) after insertion in the eye results in the appearance of glistenings.[3] Gregori et al.[4] showed that glistenings were induced by temperature changes that led to condensation of excessive water in the microvoids of the bulk material on cooling. Tognetto et al.[5] found that this opacification happens because

of scattering due to local changes in the refractive index between the IOL material and the vacuoles. Heating the IOL promotes the formation of glistenings; however, they become visible only after the temperature is lowered. Intraocular lenses with high levels of glistenings strongly scatter light; they have been shown to significantly reduce spectral transmittance, reduce resolving power (modulation transfer function), reduce contrast sensitivity, and increase glare sensitivity.[6] In some extreme cases, in addition to scattering light and causing IOL opacification (whitening),[7] glistenings lead to IOL explantation.[8]

The biomaterial of which an IOL is composed appears to play a key role in the formation of glistenings. Glistenings are more intense in materials that have voids due to incomplete polymerization or curing of the IOL material; these voids in the polymer network are potential vacuole locations. This appears to be more common in cast-molded IOLs than in IOLs that are manufactured by a lathe-milling process, in IOLs with an extremely low water content, and in IOLs in which the temperature dependency of the water content is elevated. Glistenings occur in the IOL bulk material.[9]

Findings in recent clinical studies[5] of the extent of glistenings in 2 market-leading hydrophobic acrylic IOLs, the Acrysof IQ SN60WF (Alcon Laboratories, Inc.) and the Sensar AR40e (Abbott Medical Optics, Inc.), and their clinical significance provide motivation to develop new hydrophobic materials.

This study evaluated a new-generation hydrophobic acrylic polymer, GF raw material (Physiol S.A.).[10] The material can be equilibrated in saline solution before implantation and combines the benefits of 2 families of IOL materials (ie, hydrophobic and hydrophilic acrylic). The bioadhesiveness and resistance to glistenings of the polymer composition of this material were tested and compared with those of 2 hydrophobic acrylic IOLs (Acrysof IQ SN60WF and Sensar AR40e) and 1 hydrophilic acrylic IOL (Ioflex, Mediphacos Ltda.), which served as benchmark references.

Submitted: November 21, 2011.
Final revision submitted: February 3, 2012.
Accepted: February 3, 2012.

From the Research and Development Department (Pagnoulle, Bozukova, Gobin), Physiol S.A. and the Laboratory for Histology and Cytology (Bertrand, Gillet-De Pauw), University of Liege, Liège, Belgium.

Supported by the Région Wallone (public Belgian support).

Corresponding author: Christophe Pagnoulle, PhD, Liège Science Park, Allée des Noisetiers, 4, B-4031 Liège, Belgium. E-mail: c.pagnoulle@physiol.be.

MATERIALS AND METHODS

The exact formulation of the chemically crosslinked GF hydrophobic acrylic material is proprietary, the publication of which is prevented by a pending patent.[10] To receive the Conformitée Européenne accreditation, the new hydrophobic acrylic material was tested according to the International Organization for Standardization 11979-5 and 10993-5 standards. Tests were performed to determine the (1) extractable components, (2) leachable components, (3) hydrolytic stability, (4) photolytic stability, (5) cytotoxicity of the IOL, (6) IOL extract liquid, (7) IOL preservation liquid, (8) acute systemic toxicity of the IOL extract in mice, (9) subchronic toxicity, (10) ocular irritation of the IOL extract in rabbits, (11) sensitization of the IOL extract in guinea pigs, and (12) mutagenicity. The IOLs made of the GF raw material proved to be chemically, optically, thermally, and mechanically intact after accelerated aging that mimicked 5 years of implantation at 35°C in a hydrolytic medium and 20 years of exposure to ambient light. Toxicology tests found the compatibility of this raw material to be sufficient for use in the human eye. The refractive index of the new material is 1.52 in its hydrated, equilibrated state in its saline packaging.

Glistening Evaluation

Worst-case scenario temperature fluctuation conditions were selected for the glistening test. The test was performed using a procedure similar to that described by Kato et al.[11] The IOLs were incubated in saline solution at 60°C for 1 hour, after which they were microscopically observed at 23°C. The IOLs were then reheated and observed at 60°C. Finally, they were dried at 65°C for 48 hours and observed at room temperature.

Hydrophobic Property Evaluation

The surface wettability of the test and reference IOLs were assessed via measurement of the contact angles in air and in water using a shape analysis. When a water droplet is placed on a smooth dry surface composed of a strongly hydrophilic material, it will spread over the surface and the contact angle will approach zero. Conversely, no wetting occurs for strongly hydrophobic surfaces, so the resulting contact angle is greater than 90 degrees. If there is partial wetting, the resulting contact angle reaches equilibrium in the 0- to 90-degree range depending on the material surface energy.

Similarly, when an air bubble is deposited onto the surface of a sample conditioned in a balanced salt solution, it spreads and its contact angle approaches 0 degree relative to the surface for relatively hydrophobic materials but remains spherical (>90 degrees) for hydrophilic materials.

The contact angle of water was measured at least 3 times with a DGD Fast/60 contact angle meter and Windrop++ software (Digidrop, DGD, Fast/60, GBX). For dry surfaces, the contact angles were measured by the water droplet method at a fixed time of 30 seconds with a mean deviation of ±2 degrees. Therefore, the experimental values were representative of a solid–liquid interface. The captive-bubble method was used when the IOL was hydrated (mean deviation ±3 degrees). The contact angle, which was measured at a solid–gas interface, was converted into a contact angle at a solid–liquid interface by a mirror transformation of $\theta \rightarrow 180 - \theta$.

Bioadhesiveness Evaluation

Bioadhesiveness was assessed by performing in vitro porcine LEC adhesion tests following the 11979-5 standard of the International Organization for Standardization.[12]

Porcine Lens Epithelial Cell Preparation

The porcine LECs were derived from the capsular bag of a young porcine crystalline lens. The cells were used after the second passage. A cell suspension was prepared at a concentration of 53 300 cells/mL culture medium; the culture medium contained 86% Dulbecco's Modified Eagle medium, 10% fetal bovine serum deactivated, 1% penicillin/streptomycin, 1% glutamine, 1% N-2-hydroxyethylpiperazine-N'-2-ethanesulfonic acid, and 1% sodium pyruvate.

Intraocular Lens Preparation

The bioadhesiveness of each test and reference IOL was evaluated using in vitro porcine LEC adhesion tests that were compared with a positive control reference, the bottom of a Falcon culture well. The IOLs were always tested in triplicate. The haptics of each IOL were gently removed, and the remaining optic was fixed on a purpose-made insert designed to fit a 24-well Falcon box. Preliminary immersion of the test and reference materials, including the positive control, in culture medium was aimed at bringing them to a condition that was similar to that of an implanted IOL in terms of pH, protein saturation of the surface, and salt balance. It was performed by a triple incubation for 30 minutes with 1 mL fresh culture medium at 37°C and 5% carbon dioxide (CO_2).

In Vitro Test Procedure

After removal of the preconditioning medium, 158 µL of the cell suspension was added to each well that contained an IOL and the system was incubated for 72 hours at 37°C and 5% CO_2, a time that corresponds to approximately 70% cell confluence for the positive control reference. After incubation, the culture medium was aspirated and the cells were gently rinsed 3 times with phosphate buffered saline (PBS) solution. The cells were then fixed with 4% solution of paraformaldehyde in PBS for 2 hours at 4°C, after which they were rinsed 3 times with PBS, stained with hematoxylin–eosin, and stored at 4°C until observation. Fixed cells were not stored for more than 48 hours before microscopic observation.

Characterization

The characterization was performed via observation with an Olympus IX80 inverted microscope. The proportion of the surface occupied by the cells was determined digitally.

RESULTS

Glistenings

The 2 hydrophobic benchmark reference materials became opaque (Figure 1, *A*). This was a result of phase separation between the aqueous droplets and the polymer chains, causing light scattering whose intensity depended on the density and size of the droplets.

Under the same test conditions, the Sensar AR40e IOL had surface light scattering that may be related to the distribution of water aggregates near the IOL surface according to a process that is similar to that which occurs in the formation of glistening. However, these water aggregates were much smaller than the glistening aggregates and the IOLs did not have the appearance of microvacuoles; rather they appeared to have IOL surface whitening. In contrast to the 2 reference hydrophobic materials, the IOLs made of the test GF material behaved like the hydrophilic acrylic IOL (Ioflex) and no light scattering was observed.

Drying the reference and test IOLs at 65°C for 48 hours resulted in IOLs that were transparent regardless of their composition (Figure 1, *B*). Repeating the cooling–heating cycle under less severe conditions (at 40°C) yielded similar results; however, the sizes and frequency of the vacuoles observed in the 2 reference hydrophobic IOLs were lower. On drying, any water that had been condensed within the polymer voids evaporated so neither glistening nor light scattering was observed in any of the IOLs.

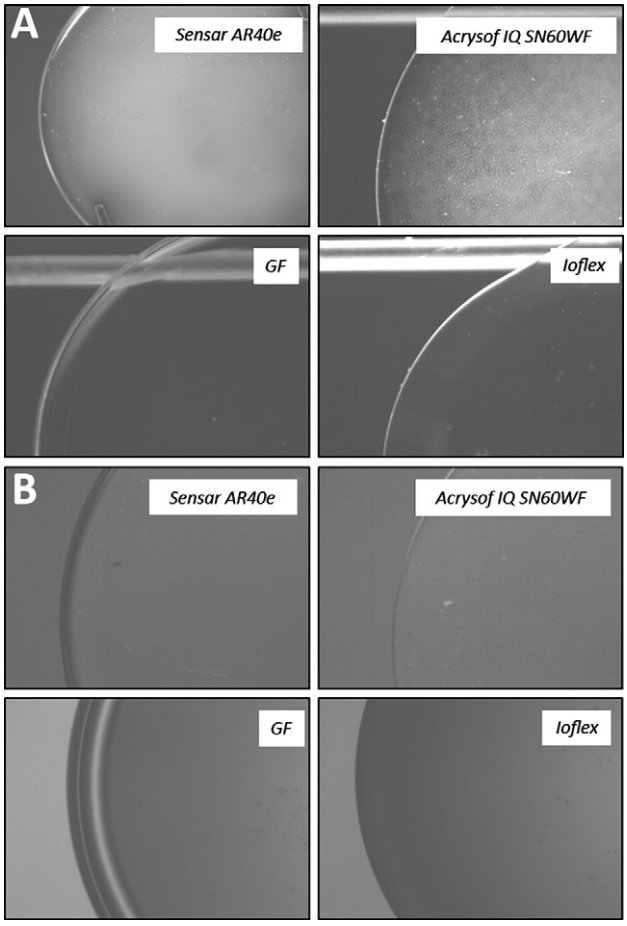

Figure 1. Evaluation of the polymer glistening and glistening reversibility. *A*: After incubation in water at 60°C for 1 hour. *B*: After drying of the hydrated IOLs at 65°C for 48 hours.

Hydrophobic Properties

The contact angles of the new test material and the 2 reference hydrophobic materials measured by the water drop method in air were in the 78- to 90-degree range (Figure 2). The Sensar AR40e material had a higher contact angle, whereas the reference hydrophilic material had a 66-degree contact angle of water. The decreases in the measured contact angles of all tested materials after hydration indicated that the hydrophobicity of the materials also diminished.

Both techniques showed that the wettability of the new material IOL surface was intermediate compared with that of the 3 reference materials with values similar to those of the Acrysof IQ SNWF60 reference. Similar tendencies would likely be observed under implantation conditions.

Bioadhesiveness

Figure 3 shows the micrographs of the IOLs after fixation and staining of the cells. Figure 4 shows the amount of surface coverage by the porcine LECs. No bioadhesiveness was observed for the hydrophilic reference IOL, which showed only 0.6% cell coverage. In contrast, the Acrysof IQ SN60WF reference had pronounced bioadhesiveness (75%) that was comparable to that of the positive control surface (74%). This observation is in good agreement with the relatively high hydrophobicity of that reference IOL material compared with that of the new test material. Although it is more hydrophobic in water than the other IOLs, the Sensar AR40e IOL showed 36% cell adhesion. The porcine LEC adhesion level (51%) on the IOL made from the new material was intermediate compared with the levels of 2 reference hydrophobic materials.

DISCUSSION

Foldable hydrophobic acrylic IOLs are obtained by the copolymerization of acrylate with a glass transition temperature of the respective homopolymer that is lower than the room temperature (glass transition temperature < room temperature) and methacrylate (glass transition temperature > room temperature).[13] These IOL materials exhibit a glass transition temperature that is just below the room temperature, which makes them foldable. By varying the nature of the ester substituent, one can modify the properties of the final material (eg, water uptake, refractive index, tackiness).

In contrast to other IOL hydrophobic compositions, which are constituted exclusively of monomers that have a poor affinity for water, the new GF formulation contains a minor amount of a hydrophilic monomer. This allows the equilibrium water content of the IOL to be maintained at a value of 4.9%. Although this amount of water is low, it is sufficient to act as a plasticizer that renders the material more foldable and

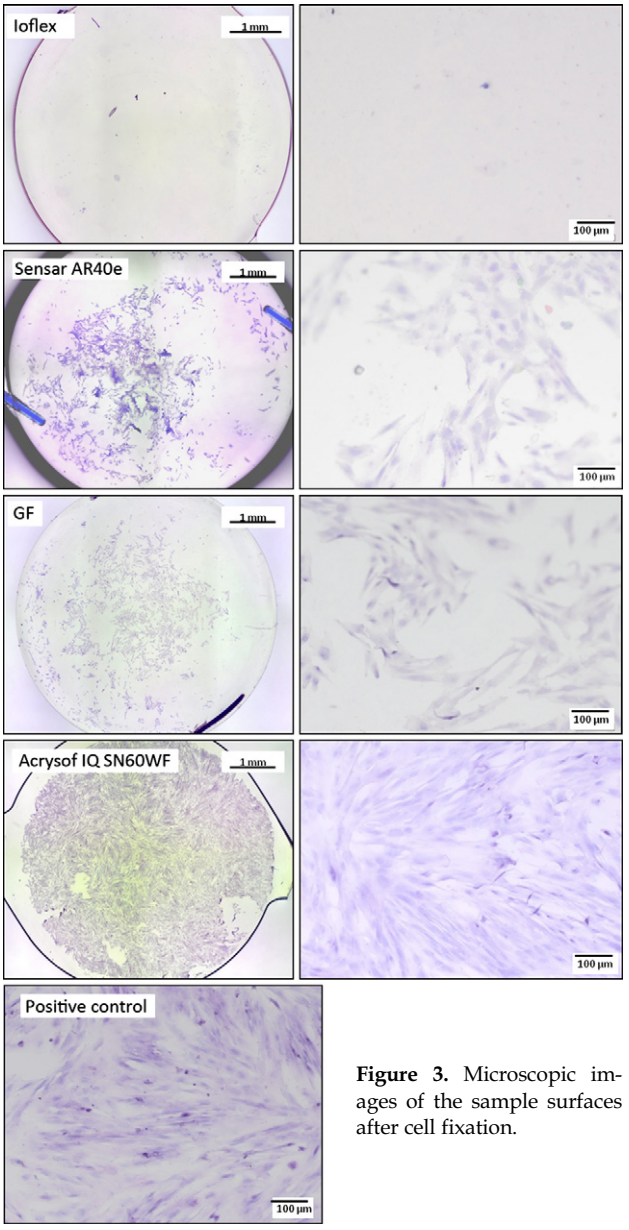

Figure 3. Microscopic images of the sample surfaces after cell fixation.

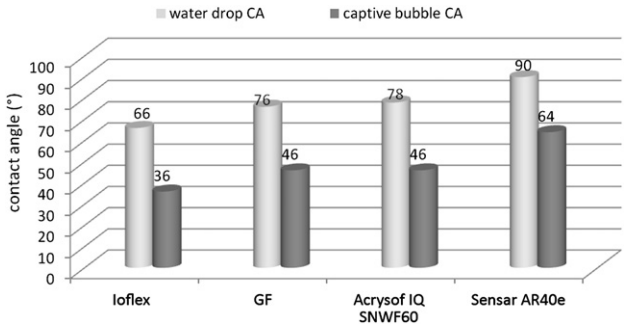

Figure 2. Contact angles of the dry (the water drop CA) and hydrated (the captive bubble CA) surface.

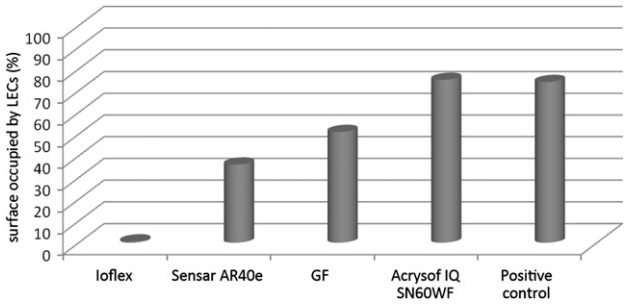

Figure 4. Comparative graph with the results of the in vitro porcine LEC adhesion test (LECs = lens epithelial cells).

compressible at the time of implantation. The foldability of the new material is especially beneficial for IOLs designed to be implanted through small incisions.

Recently, a hydrophobic acrylic IOL with 4.0% water content was launched on the market by Advanced Vision Science under the trade name XACT.[9] This IOL is packaged in 0.9% saline solution and is sterilized by gamma irradiation.[14] However, this sterilization method is known to lead to partial oxidative degradation[15] or to the formation of carcinogenic compounds within the material of the IOL or of its packaging[16] in some cases.

Another method used to sterilize hydrophobic acrylic IOLs that are packaged in their dry states, such as the Acrysof IQ SN60WF and Sensar AR40e, is ethylene oxide (ETO) sterilization. This sterilization method is associated with a risk for highly toxic residual contaminants, such as ETO or epichlorhydrine.[17,18]

In contrast, steam sterilization is a material-friendly method that has been used in the medical field for more than 50 years and is not related to harmful complications in implants or patients.[15] Therefore, this method was selected to sterilize the IOLs made of the GF material, which are packed in saline solution.

Glistenings may be explained by the infiltration of the polymer network of an IOL with an uncontrolled amount of water that results from increased chain mobility and, as a consequence, available volume at temperatures that are higher than the glass transition temperature of polymer.[8] Tognetto et al.[5] explained this opacification in terms of scattering due to local changes in the refractive index between the IOL material and the vacuoles.

The surface whitening of the Sensar AR40e IOL after incubation in water at 60°C was mostly related to phase separation that results from the intrinsic incompatibility of the fluorinated species and the aqueous phase. Meanwhile, the strong glistenings in the Acrysof IQ SN60WF IOL may be explained by 2 factors. First, it is dry conditioned and displays rapidly increasing water content on heating (0.5% at physiologic temperature[9]). Second, because it is cast molded, larger pores may form in the polymer network, which may lead to the formation of larger vacuoles in which water condenses. In contrast, the GF and the Ioflex materials are polymerized as bulky blanks in which the polymer network is expected to be better polymerized in the central part, where the IOL is lathed. The disappearance of glistenings after drying confirms the hypothesis that opacification is due to glistening formation rather than to other material changes.

It has been well documented in the scientific literature that once they have formed, glistenings evolve continuously after IOL implantation. In some cases, especially those with Acrysof references, glistenings continue to increase for as long as 2 years after surgery.[5,9] This phenomenon can be explained by the coalescence of the smaller vacuoles into larger ones.

Indeed, steam sterilization of the GF material at a temperature that is higher than 120°C temporarily enhances the mobility of the polymer network for a period that is sufficiently long to allow the absorption of the final content (4.9%) of the packaging solution. This composition is similar to that of the aqueous humor of the eye. Thus, the material reaches an equilibrated state before surgery.[9] This is in accordance with the Arrhenius law

$$k = Ae^{-Ea/RT}$$

where k is the rate constant of a reaction at temperature T and is exponential function of Ea, the activation energy, and R, the gas constant, with A being the preexponential factor and e the exponent. Therefore, these IOLs are not expected to evolve after implantation or incubation, even at an elevated temperature (60°C in the present study). The low water content of the GF material is precisely controlled through the chemical composition of the polymer. Indeed, the presence of even a minor quantity of a monomer that has an affinity for water is essential because it enhances the degree of compatibility between the hydrophobic polymer and the aqueous medium. This ensures that phase separation and light scattering do not occur.

Regarding hydrophilicity, using prolonged immersion in balanced salt solution to mimic in vivo hydration of commercial hydrophobic acrylic IOLs (Acrysof IQ SN60WF; Sensar AR40e; AF-1, Hoya Surgical Optics GmbH) has been reported to change surface wettability and decrease hydrophobicity.[9] This means that the water content of hydrophobic IOLs and the properties of these IOLs that are related to water content are prone to change after surgery.

Evaluating this hypothesis for the GF material in parallel with commercial hydrophobic and hydrophilic acrylic reference materials showed changes in the wettability of the IOLs after hydration. These changes were due to reorganization of the uppermost layers of the IOL surfaces that resulted from their intrinsic tendencies toward decreasing interface tension.

Therefore, the level of interface tension accounts for the cohesive energy that is present on a surface and that is related to an imbalance in molecular forces. In water, the polar hydrophilic groups of the polymer network tend to compensate for this extra energy by orienting toward the surface of the IOL, whereas the nonpolar species, which have poor affinity for water, move toward the underlying layer. In other words, like orients toward like.

Indeed, a higher contact angle was measured for the Sensar AR40e material in air and in water, which was most likely due to the low surface tension of the fluorinated moieties in the material composition.[9] According to Guelcher and Hollinger,[19] who describe weak cell adhesion to very hydrophobic and very hydrophilic surfaces and higher cell adhesion to intermediately hydrophobic surfaces, the hydrophilicity of the IOL surface increases in the following order: Sensar AR40e less than Acrysof IQ SN60WF less than GF less than Ioflex. This can be expected to result in a similar order of decreasing bioadhesiveness.

Despite extensive studies, the mechanism by which an IOL influences PCO remains controversial. According to the literature,[20,21] a sharp optic edge alone is not sufficient to prevent PCO. Recently, it was recognized that the bioadhesiveness of the IOL material is an important factor in the PCO rate. Hydrophobic acrylic IOLs have been shown to provoke rapid residual LEC growth along with the formation of a monolayer of cells that glues the capsular bag to the IOL surface.[3,22,23] This type of behavior was not observed for silicone or hydrophilic acrylic (hydrogel) IOLs. A cell culture test is performed in an aqueous medium; thus, one should consider the contact angle measured by the air-bubble technique, for which the material surface is in its equilibrated state. Therefore, the poor bioadhesiveness of the Ioflex IOL is not surprising because this material has a stronger hydrophilic character than the other 3 materials.[19]

In contrast, the bioadhesiveness of the GF, Sensar AR40e, and Acrysof IQ SN60WF IOL materials is expected to lead to fast, firm adhesion between the capsular bag and the IOL, resulting in a low rate of PCO. This should be confirmed by performing in vivo studies. The relatively low cell adhesion to the Sensar AR40e IOL is in accordance with the results of Nagata et al.[24]

An advantage of materials with a high degree of bioadhesiveness is the biomechanical stability of the IOL in the capsular bag. This is particularly important in the case of toric IOLs, for which a few degrees of postsurgical rotation with respect to the initial IOL position can significantly affect the optical performance of the IOL, in particular its ability to correct astigmatism. Furthermore, Nagata et al.[24] found that the risk for anterior capsule contraction was reduced with the use of hydrophobic acrylic IOLs because of their ability to form firm contact with the capsular bag and to suppress the proliferation of LECs and fibroblasts.

In conclusion, results indicate that the new-generation GF raw material for IOLs is appropriate for intracorporeal application in the human body. Its composition combines the advantages of hydrophobic and hydrophilic acrylic IOL materials. The 4.9% equilibrium water content of the new material would allow an IOL to be packaged in a physiologic solution that has a composition similar to that of the intraocular liquids before IOL implantation. Therefore, this material would not be subjected to supplementary environmental stress postoperatively, which, in contrast to benchmark references such as the Acrysof IQ SN60WF and Sensar AR40e IOL materials, promotes the absence of glistenings.

The GF raw material performed similarly to the conventional hydrophobic acrylic references in hydrophobicity and bioadhesiveness; it provoked rapid and strong LEC adhesion in vitro. This combination of a hydrophobic acrylic composition, a glistening-free optical component, and bioadhesiveness will likely lead to low PCO rates and a high level of in-the-bag biomechanical stability.

The tackiness of the GF material is being tested by atomic force microscopy and being compared with benchmark references; the results will be presented in a forthcoming publication. Meanwhile, the in vivo biocompatibility and PCO resistance for IOLs made of the new material are being studied in clinical settings and will be scientifically discussed after sufficiently long postoperative follow-up periods.

WHAT WAS KNOWN

- Hydrophobic acrylic intraocular lenses (IOLs) are associated with enhanced risk for glistening formation while they usually provoke low or no PCO. In contrast, PCO is the major postoperative complication after hydrophilic acrylic IOL implantation, which is known to resist glistening formation. Until now, a material providing a solution for both opacification types has not been developed.

WHAT THIS PAPER ADDS

- Precisely controlling the water content in the material at minimal levels allows preconditioning of the respective IOL in saline solution before implantation, vapor sterilization, and a reduced risk for glistening formation.
- Such low water content helps preserve the advantages of a hydrophobic acrylic material in terms of bioadhesiveness and a low PCO rate.

REFERENCES

1. Apple DJ. Nicholas Harold Lloyd Ridley. 10 July 1906 – 25 May 2001: elected FRS 1986. Biogr Mems Fell R Soc 2007; 53:285–307. Available at: http://rsbm.royalsocietypublishing.org/content/53/285.full.pdf. Accessed March 3, 2012
2. Nishi Y, Rabsilber TM, Limberger I-J, Reuland AJ, Auffarth GU. Influence of 360-degree enhanced optic edge design of hydrophilic acrylic intraocular lens on posterior capsule opacification. J Cataract Refract Surg 2007; 33:227–231
3. Linnola RJ. Sandwich theory: bioactivity-based explanation for posterior capsule opacification. J Cataract Refract Surg 1997; 23:1539–1542
4. Gregori NZ, Spencer TS, Mamalis N, Olson RJ. In vitro comparison of glistening formation among hydrophobic acrylic intraocular lenses. J Cataract Refract Surg 2002; 28:1262–1268
5. Tognetto D, Toto L, Sanguinetti G, Ravalico G. Glistenings in foldable intraocular lenses. J Cataract Refract Surg 2002; 28:1211–1216
6. Oshika T, Shiokawa Y, Amano S, Mitomo K. Influence of glistening on the optical quality of acrylic foldable intraocular lens. Br J Ophthalmol 2001; 85:1034–1037. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1724105/pdf/v085p01034.pdf. Accessed March 3, 2012
7. Matsushima H, Mukai K, Nagata M, Gotoh N, Matsui E, Senoo T. Analysis of surface whitening of extracted hydrophobic acrylic intraocular lenses. J Cataract Refract Surg 2009; 35:1927–1934
8. Werner L, Storsberg J, Mauger O, Brasse K, Gerl R, Müller M, Tetz M. Unusual pattern of glistening formation on a 3-piece hydrophobic acrylic intraocular lens. J Cataract Refract Surg 2008; 34:1604–1609
9. Werner L. Glistenings and surface light scattering in intraocular lenses. J Cataract Refract Surg 2010; 36:1398–1420
10. Pagnoulle C, Nolet De Brauwere Van Steeland M, inventors; PhysIOL assignee. Polymer composition for an intraocular lens. Patent WO2006/063994, December 13, 2005. Available at: http://www.wipo.int/patentscope/search/en/WO2006063994. Accessed March 3, 2012
11. Kato K, Nishida M, Yamane H, Nakamae K, Tagami Y, Tetsumoto K. Glistening formation in an AcrySof lens initiated by spinoidal decomposition of the polymer network by temperature change. J Cataract Refract Surg 2001; 27:1493–1498
12. International Organization for Standardization. Ophthalmic Implants – Intraocular Lenses – Part 5: Biocompatibility. Geneva, Switzerland, ISO, 2006; (ISO 11979-5)
13. Dimarzio EA, Gibbs JH. Glass temperature of copolymers. J Polym Sci 1959; 40(136):121–131
14. U.S. Food and Drug Administration. Summary of safety and effectiveness data. PMA P080021. Available at: http://www.accessdata.fda.gov/cdrh_docs/pdf8/P080021b.pdf. Accessed March 3, 2012
15. Davis JR. Handbook of Materials for Medical Devices. Materials Park, OH, ASM® International USA, 2003; 18–19
16. Rodríguez-Benot A, Santamaría R, Martín-Malo A, Aljama P. Sterilization procedures and biocompatibility. In: Ronco C, La Greca G, eds, Hemodialysis Technology (Contributions to Nephrology). Basle, Switzerland, Karger, 2002; 138–145
17. Furuhashi M, Miyamae T. Ethylene oxide sterilization of medical devices–with special reference to the sporicidal activity and residual concentration of ethylene oxide and its secondary products. Bull Tokyo Med Dent Univ 1982; 29:23–35
18. Buben I, Melichercíková V, Novotná N, Svitáková R. Problems associated with sterilization using ethylene oxide. Residues in treated materials. Cent Eur J Public Health 1999; 7:197–202
19. Harbers GM, Grainger DW. Cell-material interactions: fundamental design issues for tissue engineering and clinical considerations. In: Guelcher SA, Hollinger JO, eds, An Introduction to Biomaterials. Boca Raton, FL, Taylor Francis Group, 2006; 15–45
20. Nishi O, Nishi K. Effect of the optic size of a single-piece acrylic intraocular lens on posterior capsule opacification. J Cataract Refract Surg 2003; 29:348–353
21. Nishi O, Nishi K, Akura J. Speed of capsular bend formation ati the optic edge of acrylic, silicone, and poly(methyl methacrylate) lenses. J Cataract Refract Surg 2002; 28:431–437
22. Lombardo M, Carbone G, Lombardo G, De Santo MP, Barberi R. Analysis of intraocular lens surface adhesiveness by atomic force microscopy. J Cataract Refract Surg 2009; 35:1266–1272
23. Küçüksümer Y, Bayraktar Ş, Şahin S, Yılmaz ÖF. Posterior capsule opacification 3 years after implantation of an AcrySof and a MemoryLens in fellow eyes. J Cataract Refract Surg 2000; 26:1176–1182
24. Nagata M, Matsushima H, Mukai K, Terauchi W, Gotoh N, Matsui E. Comparison of anterior capsule contraction between 5 foldable intraocular lens models. J Cataract Refract Surg 2008; 34:1495–1498